At pages 2-3 of the Office Action, claims 1-4, 7-10, 28-30 and 32 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 and 14-25 of copending U.S. Patent Application No. 10/639,900. For brevity, reference is made to pages 2-3 of the Office Action for the complete reasons for rejection.

While Applicants respectfully disagree with and traverse this rejection, a terminal disclaimer is submitted with this response to terminally disclaim the terminal part of the statutory term of any patent granted on the present application that would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. § 154 to 156 and 173, as shortened by any terminal disclaimer filed prior to the grant, of any patent granted on pending U.S. Patent Application No. 10/639,900, subject to the conditions noted in the terminal disclaimer.

Accordingly, Applicants respectfully request that the rejection of claims 1-4, 7-10, 28-30 and 32 under the judicially created doctrine of obviousness-type double patenting, be reconsidered and withdrawn.

At pages 3-7 of the Office Action, claims 1-4, 7-10, 28-30 and 32 have been rejected under 35 U.S.C. §103(a) as obvious over U.S. Patent No. 5,846,966 ("Rosenblum et al.") in view of U.S Patent No. 5,698,527 ("Kim") and WO 2000/38725 ("Keller et al.").

For brevity, the reasons for rejection are not repeated herein but reference is made to the outstanding Office Action.

Applicants respectfully traverse this rejection and request that the rejection be reconsidered and withdrawn.

When making a rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing a prima facie case of obviousness. In re Fritch, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992).

The Examiner can satisfy this burden only by showing an objective teaching in the prior art, or knowledge generally available to one of ordinary skill in the art, which would lead an individual to combine the relevant teachings of the references [and/or the knowledge] in the manner suggested by the Examiner. Id.; In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988).

The mere fact that the prior art could be modified does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d at 1784; In re Laskowski, 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989); In re Gordon, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984).

"It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious....'[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.'" In re Fritch, 23 U.S.P.Q.2d at 1784 (quoting In re Fine, 5 U.S.P.Q.2d at 1600).

"The ultimate determination of patentability must be based on consideration of the entire record, by a preponderance of evidence, with due consideration to the persuasiveness of any arguments and any secondary evidence." Manual of Patent Examining Procedure, (Rev. 1, Feb. 2003) § 716.01(d) and In re Oetiker, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992).

As shown in Table 1 of the present application, Compound XII (a substituted azetidinone cholesterol absorption inhibitor) reduced plasma cholesterol levels and the accumulation of hepatic cholesteryl esters in the cholesterol-fed hamsters. Niacin reduced plasma triglyceride levels, but did not significantly reduce the cholesterol levels. The combination of Compound XII and niacin resulted in reductions in plasma and hepatic cholesterol levels, as well as plasma triglycerides (Table 1). These results indicate that the combination of the cholesterol absorption inhibitor of Compound XII and niacin can have additive effects on treating hyperlipidemia in male Golden Syrian hamsters, by reducing both cholesterol and triglyceride levels.

Rosenblum et al. do not suggest or disclose the combination of ezetimibe and nicotinic acid. Rosenblum et al. do not suggest or disclose the desirability of a 10 milligram dosage of ezetimibe.

Kim discloses steroidal glycoside cholesterol absorption inhibitors that can be administered in combination with niacin, but does not suggest or disclose combining ezetimibe with niacin or the desirability of the claimed amount of 10 milligrams of ezetimibe. Ezetimibe is not a steroidal glycoside. The steroidal glycosides disclosed by Kim are structurally very dissimilar to the

presently claimed substituted azetidinone compound ezetimibe. Given their large molecular size, it is unlikely that Kim's steroidal glycosides are absorbed through the intestine. In contrast, multiple peaks in plasma concentration-time profiles suggest that the glucuronide conjugate of ezetimibe undergoes enterohepatic recycling before elimination. See ZETIA™ (ezetimibe) Tablets Package Insert at column 2 (Merck/Schering-Plough Pharmaceuticals) (October 2002), included in the Information Disclosure Statement of August 30, 2004. This enterohepatic recycling can enhance efficacy.

Kim's steroidal glycoside compounds have not been commercialized by Merck & Co., Inc. (the assignee of the Kim patent). Rather, Merck is the joint venture partner of Schering-Plough (assignee of the present application) in marketing the cholesterol absorption inhibitor ZETIA™ ezetimibe formulation. ZETIA was launched in late 2002 and global sales of ZETIA in the 2003 fourth quarter totaled $165 million, with U.S. sales of $144 million. Press Release: Schering-Plough Reports Financial Results for 2003 Fourth Quarter, Full Year Monday January 26, 6:33 am ET.

"[S]econdary considerations such as ... commercial success, long-felt need, failure of others ... are relevant to the issue of obviousness and must be considered in every case in which they are present. When evidence of any of these secondary considerations is submitted, the examiner must evaluate the evidence." M.P.E.P. § 2141 (Rev'd May 2004). Applicants respectfully request that the above information regarding commercial success, long-felt need, failure of others be considered by the Examiner.

Applicants respectfully request that the Examiner return an initialed PTO-1449 form for the Information Disclosure Statement submitted herewith and each of the Information Disclosure Statements submitted on October 28, 2003, April 12, 2004 and May 13, 2004, indicating that the Examiner has considered each of the references cited therein.

In view of the foregoing remarks, it is respectfully submitted that all of the pending claims in the present application are distinguishable from the cited prior art. Accordingly, reconsideration and withdrawal of the rejection and an early Notice of Allowance are respectfully requested.

Respectfully submitted,

Date: January 11, 2005

Ann Marie Cannoni
Registration No. 35,972
WEBB ZIESENHEIM LOGSDON
ORKIN & HANSON, P.C.
700 Koppers Building
436 Seventh Avenue
Pittsburgh, PA 15219
Phone: (412) 471-8815
Fax: (412) 471-4094
E-mail: acannoni@webblaw.com